IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of)
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ROGER P. EKINS)
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Serial No. 08/447,820)
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Filed: May 23, 1995)
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For: DETERMINATION OF AMBIENT CONCENTRATIONS OF SEVERAL ANALYTES

Examiner: M. Woodward

Group Art Unit: 1815

DECLARATION OF STUART WOODHEAD

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Dr Stuart Woodhead, declare as follows:

1. I am Reader in Endocrine Biochemistry at the University of Wales College of Medicine, Cardiff, UK and have been active in the immunodiagnostics field for the last 30 years. My academic CV and list of publications is attached to this declaration.

2. I have been asked to comment on the instant application and the state of the art at the priority date in 1987. In particular, I have been asked to provide an opinion on the objections raised by the Examiner in light of WO94/01031 (Ekins '031) and US Patent No 4,385,126 (Chen et al '126). I have reviewed the above application, the Ekins '031 and Chen et al '126 references, the declaration of Dr Johann Berger and the objections raised by the Examiner in the Final Rejection of 2 September 1997 and the Advisory Action of 10 December 1997.

3. The instant application describes an assay in which binding agent specific for an analyte is immobilised at high density, e.g. as microspots, in an amount less than 0.1V/K moles. The application describes that this approach provides an assay which can provide highly sensitive results and assays which are sample-volume independent and independent of the amount of binding agent used.

4. Much of my own work has been directed at the development of high sensitivity immunoassays. In 1984, for example, I described one of the earliest ultra-sensitive assays for human thyrotrophin which was based on the use of antibodies labelled with a chemiluminescent molecule. At that time, I had appreciated that immunometric assays based on high specific activity labels could provide highly sensitive analytical methods. My convictions were supported totally by the work of Ekins who had provided the theoretical analysis to validate this approach. At that time, however, it was universally

accepted that in order to optimise immunometric assays, it was necessary to use an excess of binding reagent in order to "capture" as much of the analyte as possible. Indeed, in 1980, Ekins had pointed out that the immunometric assays devised by myself and my colleagues would perform optimally as the antibody concentration approached infinity. In later years, when I heard Ekins describe his method for the measurement of ambient analyte concentrations, it seemed to me that while the concept was attractive, the requirement to reduce the amount of binding reagent in such assays would inherently restrict their application to situations where high sensitivity was not required. I would thus contend that it would be far from obvious that the use of immobilised microspots of small amounts of antibody could actually provide a basis for highly sensitive immunoassays. To my mind such a possibility is not disclosed by Ekins '031.

5. In both the Final Rejection and the Advisory Action, the Examiner contends that the claimed invention is obvious as a person of ordinary skill in the art would arrive at it by optimising the results and equations set out in Ekins '031. The equation and teaching in Ekins '031 relate to the construction of assays which are sample-volume independent. While this is in itself a desirable goal, the equations in Ekins '031 are not concerned with the issue of assay sensitivity and so they do not suggest that, under certain circumstances, using a small amount of binding agent could enhance sensitivity. Thus, in my opinion, the disclosure in Ekins '031 does not teach or suggest the claimed invention to a person of ordinary skill in the art.

6. Further, Chen et al '126 does not make up for the deficiency of the disclosure of Ekins '031, as Chen et al '126 does not contain any disclosure concerning immobilizing less than 0.1 V/K moles of binding agent as a microspot, nor the advantages produced by this feature of the assay of the above application. I note in this regard that Chen et al fails to disclose or suggest that the use of such a small amount of binding agent in an assay with a reaction time as short as assays of conventional design that employ large amounts of antibody could provide comparable or even better sensitivity.

7. In summary, the equations in Ekins '031 do not relate to assay sensitivity and so it is not clear to me how they could be optimised by a person of ordinary skill in the art to arrive at the claimed invention. Further, at the priority date, there was no incentive for the skilled person trying to produce a sensitive assay to reduce the amount of binding agent used as this would run contrary to the generally accepted views in the art at that time. Further, I do not believe that a person of ordinary skill in the art would have been motivated to apply the combined disclosures of Ekins '031 and Chen et al '126 in such a way as to arrive at the assay of the above application.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001, Title 18 of the United States Code, and that such wilful false statements may jeopardize the validity of this application or any patent issued thereon.

Date: February 20, 1998 Signed: J N Woodhead